

Table 1 Frequencies of HLA Class I Alleles That are Known to Serve as HIV CTL Restriction Elements in Four Populations

HLA Alleles	Frequencies*			
	African Americans	USA Caucasians	North American Indians	Thais
A2	16.7	28.3	25.5	25.5
A3	8.9	12.2	2.9	1.5
A11	2.3	5.5	1.0	32.5
A24	4.7	9.6	19.6	14.6
A28	10.9	4.5	6.9	0.8
A30	9.5	2.6	2.0	1.1
A31	1.7	2.0	27.5	1.7
A32	1.0	5.1	2.0	0.2
A33	8.1	1.0	1.0	13.6
B7	8.3	10.0	3.9	2.7
B8	3.2	10.0	5.6	0.2
B12 (44)	6.2	10.4	3.9	5.4
B13	0.9	3.0	1.0	9.3
B14	3.0	4.1	2.9	0.4
B17	10.9	4.9	1.0	8.1
B18	3.3	4.9	1.0	2.5
B27	1.6	4.1	2.9	6.0
B35	7.7	8.5	18.6	2.5
B37	0.9	2.2	0.0	1.4
B52	1.1	1.2	2.9	3.1
B53	12.8	0.8	0.0	0.0
B57	4.2	3.9	1.0	5.2
B60	1.3	4.5	2.9	8.3
B62	1.4	5.5	4.9	5.0
Cw3	9.6	12.6	22.4	15
Cw4	21.0	9.8	15.4	6

*Frequencies for HLA-A and HLA-B alleles are taken from HLA 1991 [21], HLA-C for African Americans and USA Caucasians are taken from Histocompatibility Testing 1984 [19], HLA-C for North American Indians from Williams and McAuley, 1992 [22], and HLA-C for Thais from the Proceedings of the Second Asia and Oceania Histocompatibility Workshop Conference [23].

Table 2 Proportion of each of the four populations that would be predicted to present peptides to the immune system

Population	HLA Restriction Elements Chosen	HIV Protein	Epitope Location	Epitope
a) African Americans	A2, A3, A11, B35	nef	73-82	QVPLRPMTYK
	A28, B14	gp41	583-592	VERYLKDQQL
	A30, B8	gp41	844-863	RRIRQGLERALL
	B17, B37	nef	117-128	TQGYFPQWQNYT
	Cw4	gp120	576-383	(S) FNCGGEFF
<i>(Proportion of African Americans expected to present these 5 epitopes is 92.3%)</i>				
b) USA Caucasians	A2, A3, A11, B35	nef	73-82	QVPLRPMTYK
	A30, B8	gp41	844-863	RRIRQGLERALL
	B7	gp120	302-312*	RPNNNTRKSI
		nef	126-138*	NYTPGPGVRYPLT
	B12	p24	169-184	IPMFSALSEGATPQDL
<i>(Proportion of USA Caucasians expected to present these 4 epitopes is 90.2%)</i>				
c) North American Indians	A2, A3, A11, B35	nef	73-82	QVPLRPMTYK
	A24	gp41	584-591*	YLKDQQL
		nef	120-144*	YFPDWQNYTPGPGIRYPLTFGCWCYK
	A31	gp41	770-780	RLRDLILLIVTR
<i>(Proportion of North American Indians expected to present these 3 epitopes is 96.4%)</i>				
d) Thais	A2, A3, A11, B35	nef	73-82	QVPLRPMTYK
	A24	gp41	584-591*	YLKDQQL
		nef	120-144*	YFPDWQNYTPGPGIRYPLTFGCWCYK
<i>(Proportion of Thais expected to present these 2 epitopes is 93.6%)</i>				
e) African Americans	A2, A3, A11, B35	nef	73-82	QVPLRPMTYK
USA Caucasians	A28, B14	gp41	583-592	VERYLKDQQL
North American Indians	A30, B8	gp41	844-863	RRIRQGLERALL
Thais	B17, B37	nef	117-128	TQGYFPQWQNYT
	Cw4	gp120	376-383	(S) FNCGGEFF
	B7	gp120	302-312*	RPNNNTRKSI
		nef	126-138*	NYTPGPGVRYPLT
	B12	p24	169-184	IPMFSALSEGATPQDL
	A31	gp41	770-780	RLRDLILLIVTR
	A24	gp41	584-591*	YLKDQQL
		nef	120-144*	YFPDWQNYTPGPGIRYPLTFGCWCYK

(Proportions of African Americans, USA Caucasians, North American Indians, and Thais expected to present these 9 epitopes are 95.4%, 97.5%, 99.4%, and 97.2%, respectively)

*The criteria upon which choices among peptides should be made are not yet known. It may be important to choose peptides that have been reported to be immunogenic in non-progressors to AIDS or that have been reported to induce immunodominant anti-HIV T-cell responses.

TABLE 3

Th-CTL Peptide Prototype Vaccine Immunogens for Testing in Either Mice, Rhesus Macaque or Human

Vaccine number	Name of Peptides	Species in which to be studied	Amino acid sequence	Restricting elements for CTL epitope
1.	Mouse HIV-1 Th-CTL epitopes		Th - CTL	
	A-Th/A-CTL	Mouse	HAGP LAPGQMREPRG-KQIINMWQEVGKAMYA	H-2 ^d
	B-Th/B-CTL	Mouse	KEKVYLAWPAAHKGIG-HYAPPIGGQI	H-2 K ^b
	C-Th/C-CTL	Mouse	QLLF IIFRIGCRHSR-DRVIEVQGAYRAIR	H-2 ^d (D ^b)
	D-Th/D-CTL	Mouse	EQMHEDIISLWQSL-RIHIGPGAFYTTKV	H-2 D ^b
3.	Macaque SIV/HIV-1 Th-CTL epitopes		Th - CTL	
	Th1/CTL/SIV Gag	Macaque	ELYKYVVKIEPLGVAPTKA-CTPYDINQM	Mamu-A*01
	Th2/CTL/SIV Pol	Macaque	VSTVQCTHGIRPVVSTQLLL-STPPLVRL	Mamu-A*01
	Th3/CTL/HIV-1 Env	Macaque	STSIRGKVQKEYAFFYKLDI-YAPPIGGQI	Mamu-A*01
5.	Macaque SIV/HIV-1 Th-CTL p11c epitopes variants		Th - CTL	
	Th1/CTL/SIV Gag	Macaque	ELYKYVVKIEPLGVAPTKA-CTPYDINQM	Mamu-A*01
	Th2/CTL/SIV Gag/p11c/I-Y	Macaque	VSTVQCTHGIRPVVSTQLLL-CTPYDINQM	Mamu-A*01
	Th3/CTL/SIV Gag/p11c/I-A	Macaque	STSIRGKVQKEYAFFYKLDI-CTPYDINQM	Mamu-A*01
	Th4/CTL/SIV Gag/p11c/I-D	Macaque	EYAFFYKLDIIPIDNDTTSY-CTPYDINQM	Mamu-A*01
	Th5/CTL/SIV Gag/p11c/I-K	Macaque	REQFGNNTIIFKQSSGGDPE-CTPYDINQM	Mamu-A*01
6.	Human HIV-1 Th-CTL overlapping epitopes		Th - CTL	
	A-Th/A-CTL	Human	KQIINMWQEVGKAMYA-KAFSPEVIMPF	HLA B57.B53
	B-Th/B-CTL	Human	YKRWIILGLNKIVRMYS-NPPIPVGEIYKRWI-ILGLNKIVRMYSPTSI	HLA B35.B8.B27.A33.Bw62.B52
	C-Th/C-CTL	Human	DRVIEVQGAYRAIR-VGPPVRQVPLRPMTYK	HLA A1.B7.B8.B35.A11.A2.A3.A31
	D-Th/D-CTL	Human	ASLWNWFNITNWLWY-WVYHTQGFPPDQWNYTP	HLA B7.B57.A1.B8.B13.B35
8.	Human HIV-1 Th-dominant/subdominant CTL epitopes		Th - CTL	
	A-Th/E-CTL	Human	KQIINMWQEVGKAMYA-SLYNTVATL	HLA A2
	B-Th/F-CTL	Human	YKRWIILGLNKIVRMYS-KIRLRPGGK	HLA A3
	C-Th/G-CTL	Human	DRVIEVQGAYRAIR-KRWIILGLNK	HLA B27
	D-Th/H-CTL	Human	ASLWNWFNITNWLWY-GGAKKYKL	HLA B8
	E-Th/I-CTL		MREPRGSKLAGTTST-ERYLADQQL	HLA B14
10.	Human HIV-1 Th-CTL p17 epitope (A2 Variants)		Th - CTL	
	B-Th/E-CTL	Human	YKRWIILGLNKIVRMYS-SLYNTVATL	HLA A2
	C-Th/J-CTL	Human	DRVIEVQGAYRAIR-SLYNTVATL	HLA A2
	A-Th/K-CTL	Human	KQIINMWQEVGKAMYA-SLYNAVATL	HLA A2
	D-Th/L-CTL	Human	ASLWNWFNITNWLWY-SLYNTVAVL	HLA A2
	E-Th/M-CTL	Human	MREPRGSKLAGTTST-SLYNTLAVL	HLA A2

Vaccine number	Name of Peptides	Amino acid sequence	Restricting elements for CTL epitope
11.	Human HIV-1 Th-CTL overlapping epitopes	Th - CTL	
	A*-Th/J-CTL	KQIINMWQVVGKAMYA-GQMVHQAI SPRTLNAWVKVV	A2, A202, A5, B7, B14, B57, B5701, B5801, B02, Cw3
	A*-Th/K-CTL	KQIINMWQVVGKAMYA-ATPQDLNTMLNTVGGHQAAMQMLKETINEEAAEW	A2, A25, A26, B7, B12, B14, B1402, B27, B39, B52, B53, B57, B58, B8101, Cw8, Cw0102
	A*-Th/L-CTL	KQIINMWQVVGKAMYA-GPKEPFRDYVDRFYKTLRAEQASQEVKNWMT	A2, A202, A5, A24, A2402, A25, A26, A33, B7, B8, B12, B14, B35, B39, B44, B52, B53Bw62, B27, B2705, B57, B5701, B70, B71, Bw62, Cw3, Cw8, Cw0401
	A*-Th/M-CTL	KQIINMWQVVGKAMYA-KIRLRPGGKKYKLVHVGSEELRSLYNTVATLYCVHQRI	A1, A2, A3, A3.1, A03, A11, A23, A24, A0201, A2402, B8, B27, B42, B62, Bw62, Cw4

A*-Th=C4E9V

Table 4

Linear Array of Th-CTL Epitopes To Be Expressed in Modified Vaccinia Ankara

MVA-1) HIV-1 mouse Th-CTL epitopes in

A-Th/p24 (H-2 b) A-CTL/gp120 (H-2 ab1) B-Th/RT (H2 afk) B-CTL/gp120 (H-2K d1)
 HAGPIAPQMREPRG--KQIINMWQEVGKAMYA---KEKVYLAWVPAHKGIG---MYAPPIGGQI-
 C-Th/vor (H-2 d) C-CTL/gp41 (H-2 dpuq (D d) D-Th/gp120 (H-2 d) D-CTL/gp120 (H-2D d)
 --QLLFIFHFRIIGCRHSR---DRVIEVVQGAYRAIR---EQMHEDIISLWDQSL---RIHIGPGRAFYTTKN

MVA-2) p55/gag + the same HIV-1 mouse Th-CTL epitopes in MVA-1

MVA-3) HIV-1/SIV Th-CTL epitopes in

Th1/gp120/DRB*w201 CTL/SIV Gag (Mamu-A*01) Th2/DRBI*5406 CTL/SIV Pol (Mamu-A*01)
 ELYKYKVVVKIEPLGVAPTKA---CTPYDINQML---VSTVQCTHGIRPVVSTQQLL---STPPLVRL-
 Th3/gp120 CTL/HIV-1 Env (Mamu-A*01)
 --STSRGKVQKEYAFFYKLDI---YAPPISGQ-

MVA-4) p55/gag + the same HIV-1/SIV Th-CTL epitopes in MVA-3

MVA-5) SIV Th-CTL p11c epitope variants in

Th1/DRB*w201 CTL/SIV Gag (Mamu-A*01) Th2/DRBI*5406 CTL/Gag/p11c/I-Y
 ELYKYKVVVKIEPLGVAPTKA---CTPYDINQML---VSTVQCTHGIRPVVSTQQLL---CTPYDINQML-
 Th3/P14 CTL/Gag/p11c/I-A Th4/P15 CTL/Gag/p11c/I-D
 --STSRGKVQKEYAFFYKLDI---CTPYDANQML---YAFFYKLDIIPIDNDTTSY---CTPYDINQML-
 Th5/P33 CTL/Gag/p11c/I-K
 --REQFGNNKTIIFKQSSGGDPE---CTPYDINQML

MVA-6) HIV-1 human Th-CTL overlapping epitopes in

A-Th/gp120/422-437 A-CTL/p24/30-40 B-Th/GTH1/130-146 B-CTL/P24/121-150
 KQIINMWQEVGKAMYA---KAFSPFVPMF---YKRWIILGLNKIVRMYS---NPPIPVGZIVYKRWIILGLNKIVRMYSPTSI-
 C-Th/gp41/317-331 C-CTL/Net/64-80 D-Th/gp41/157-171 D-CTL/Net/111-127
 --DRVIEVVQGAYRAIR---VGFPVRPQVPLRPMTYK---ASLWNWFNITNWLWY---WVYHTQGFFPDWQNYTF

Restricting elements for CTL epitopes:

A-CTL epitope=HLA B57/B58; B-CTL epitope=HLA B35/B8/B27/A33/Bw62/B52;

C-CTL epitope=HLA A11/B7/B8/B35/A11/A2/A3/A31; D-CTL epitope=HLA B7/B57/A1/B8/B19/B35.

MVA-7) p55 gag + the same HIV-1 human Th-CTL overlapping epitopes in MVA-6

MVA-8) HIV-1 Th-dominant/subdominant CTL epitopes in

A-Th/C4/422-437 E-CTL/p17/77-85(A2) B-Th/GTH1/130-146 F-CTL/p17/18-26(A3) C-Th/gp41/317-331
 KQIINMWQEVGKAMYA---SLYNTVATL---YKRWIILGLNKIVRMYS---KIRLRPGGK---DRVIEVVQGAYRAIR-
 G-CTL/p24/131-140(B27) D-Th/gp41/157-171 H-CTL/p17/24-31(B8) E-Th/p24/96-110 I-CTL/gp41/74-82(B14)
 --KRWIILGLNK---ASLWNWFNITNWLWY---GGKXKYKL---MREPRGSKIAGTTST---ERYLKDQQL-

MVA-9) p55/gag + the same HIV-1 Th-dominant/subdominant CTL epitopes in MVA-8

MVA-10) HIV-1 Th-CTL A2 p17 epitope (A2 Variants) in

B-Th/GTH1/130-146 E-CTL/p17/77-85(A2) C-Th/gp41/317-331 J-CTL/P17/Consensus A A-Th/C4/422-437
 YKRWIILGLNKIVRMYS---SLYNTVATL---DRVIEVVQGAYRAIR---SLYNTVATL---KQIINMWQEVGKAMYA-
 K-CTL/P17/RF D-Th/gp41/157-171 L-CTL/P17/Consensus F E-Th/p24/96-110 M-CTL/P17/V1525
 --SLYNTVATL---ASLWNWFNITNWLWY---SLYNTVATL---MREPRGSKIAGTTST---SLFNLLAVL

Table 5

HIV Polyvalent C4-V3 Peptides Studied in Guinea Pigs, Primates Or In Humans		
Peptide	gp120 C4 Region	gp120 V3 Region
C4-V3MN	KQIINMWQEVGKAMYATRPNYNKRRIHIGPGRAFYTTK	
C4-V3RF	KQIINMWQEVGKAMYATRPNNNTRKSITKGPRVIYATG	
C4-V3EV91	KQIINMWQEVGKAMYATRPNNTRKSIPIGPGRAFIATS	
C4-V3CanOA	KQIINMWQEVGKAMYATRPNNTRKSIHMGPGKAFYTTG	
C4E9G-V3RF	KQIINMWQGVGKAMYATRPNNNTRKSITKGPRVIYATG	
C4E9V-V3RF	KQIINMWQVVGKAMYATRPNNNTRKSITKGPRVIYATG	
C4K12E-V3RF	KQIINMWQEVGEAMYATRPNNNTRKSITKGPRVIYATG	
Sequences from the Los Alamos Database.		

TABLE 6

Th-CTL Peptide Prototype Vaccine Immunogens derived from HIV-1 gag

Vaccine number	Name of Peptides	Amino acid sequence	Restricting elements for CTL epitope
	Human HIV-1 Th-CTL overlapping epitopes	Th - CTL	
6	A-Th/A-CTL	KQIINMWQEVGKAMYA-KAFSPEVIPMF	B57,B58
6	B-Th/B-CTL	YKRWIILGLNKIVRMYS-NPPIPVGEIYKRWIILGLNKIVRMYSPTSI	B35,B8,B27,A33,Bw62,B52
11	A*-Th/J-CTL	KQIINMWQVVGKAMYA-GQMVHQAISPTLNWVKVV	A2, A202,A5, B7, B14, B57, B5701, B5801, B02, Cw3
11	A*-Th/K-CTL	KQIINMWQVVGKAMYA-ATPQDLNTMLNTVGGHQAAMQMLKETINEEAAEW	A2,A25, A26, B7, B12, B14, B1402, B27, B39, B52, B53, B57, B58, B8101, Cw8, Cw0102
11	A*-Th/L-CTL	KQIINMWQVVGKAMYA-GPKEPFRDYVDRFYKTLRAEQASQEVKNWMT	A2,A202,A5,A24,A2402,A25,A26, A33, B7, B8,B12, B14 B35,B39, B44, B52, B53Bw62, B27, B2705, B57, B5701, B70, B71.Bw62, Cw3, Cw8, Cw0401
11	A*-Th/M-CTL	KQIINMWQVVGKAMYA-KIRLRPGGKKKKYKLKHIVWGSEELRSYNTVATLYCVHQRI	A1,A2,A3, A3.1,A03, A11, A23, A24, A0201, A2402, B8, B27, B42, B62, Bw62, Cw4

A*-Th=C4E9V

Summary of restricting elements for CTL epitopes in Vaccines A, B, J, K, L and M

A: A1, A2 (02), (01), A3, A3.1, A5, A11, A23, A24 (02), A25, A26 and A33.

B: B7, B8, B12, B14 (02), B27 (05), B35, B39, B42, B44, B52, B53, B57 (01), B58 (01) B62 (w62), B70 and B71.

C: Cw3, Cw4, Cw0401 and Cw8.

HIV Th/CTL vaccine ABJKLM